Original Effective Date: 05/01/2021
Current Effective Date: 09/29/2024
Last P&T Approval/Version: 07/31/2024
Next Review Due By: 07/2025
Policy Number: C22214-A

Imcivree (setmelanotide) NC

PRODUCTS AFFECTED

Imcivree (setmelanotide)

COVERAGE POLICY

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Coverage Guideline must be read in its entirety to determine coverage eligibility, if any. This Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide Molina Healthcare complete medical rationale when requesting any exceptions to these guidelines.

Documentation Requirements:
Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

DIAGNOSIS:
Chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to proopiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency, and Bardet-Biedl syndrome (BBS)

REQUIRED MEDICAL INFORMATION:
All uses of Imcivree (setmelanotide) are excluded from coverage per Social Security 1927(d)(2)(A*)*

A State may exclude or otherwise restrict coverage of a covered outpatient drug if the drug is contained in the list:
Agents when used for anorexia, weight loss, or weight gain.
Agents when used to promote fertility.
Agents when used for cosmetic purposes or hair growth.
Agents when used for the symptomatic relief of cough and colds.
Agents when used to promote smoking cessation.
Prescription vitamins and mineral products, except prenatal vitamins and fluoride preparations.
Nonprescription drugs, except, in the case of pregnant women when recommended in accordance with the Guideline referred to in section 1905(bb)(2)(A), agents approved by the Food and Drug

Administration under the over-the-counter monograph process for purposes of promoting, and when used to promote, tobacco cessation.
Covered outpatient drugs which the manufacturer seeks to require as a condition of sale that associated tests or monitoring services be purchased exclusively from the manufacturer or its designee.
Barbiturates.
Benzodiazepines.
Agents when used for the treatment of sexual or erectile dysfunction, unless such agents are used to treat a condition, other than sexual or erectile dysfunction, for which the agents have been approved by the Food and Drug Administration.

Weight loss drugs are benefit exclusions as outlined in the Marketplace Evidence of Coverage.

CONTINUATION OF THERAPY:
N/A

DURATION OF APPROVAL:
N/A

PRESCRIBER REQUIREMENTS:
N/A

AGE RESTRICTIONS:
N/A

QUANTITY:
N/A

PLACE OF ADMINISTRATION:
N/A

DRUG INFORMATION

ROUTE OF ADMINISTRATION:
Subcutaneous

DRUG CLASS:
Melanocortin 4 (MC4) Receptor Agonists

FDA-APPROVED USES:
Indicated for chronic weight management in adult and pediatric patients 6 years of age and older with monogenic or syndromic obesity due to pro-opiomelanocortin (POMC), proprotein convertase subtilisin/kexin type 1 (PCSK1), or leptin receptor (LEPR) deficiency as determined by an FDA-approved test demonstrating variants in POMC, PCSK1, or LEPR genes that are interpreted as pathogenic, likely pathogenic, or of uncertain significance (VUS), and Bardet-Biedl syndrome (BBS).

Limitations of Use: Imcivree is not indicated for the treatment of patients with the following conditions as Imcivree would not be expected to be effective:
• Obesity due to suspected POMC, PCSK1, or LEPR deficiency with POMC, PCSK1, or LEPR variants classified as benign or likely benign.
• Other types of obesity not related to POMC, PCSK1 or LEPR deficiency, or BBS, including obesity associated with other genetic syndromes and general (polygenic) obesity.

COMPENDIAL APPROVED OFF-LABELED USES:

Drug and Biologic Coverage Criteria
None

APPENDIX

APPENDIX:
None

BACKGROUND AND OTHER CONSIDERATIONS

BACKGROUND:
Obesity is a very common condition worldwide that has various possible etiologies. There is a growing body of literature that describes rare genetic variants implicated in the melanocortin pathway that cause severe obesity. This pathway consists of neurons that run through the hypothalamus and activate the MC4R and is responsible for regulating hunger and energy expenditure. The POMC-, PCSK1-, and LEPR-expressing neurons are all involved in this pathway. Biallelic variants in *POMC*, *PCSK1*, and *LEPR* are rare genetic disorders that can result in deficiencies that cause obesity.
Due to a lack of awareness and overlapping clinical features with other causes of obesity, POMC, PCSK1, and LEPR deficiencies remain underdiagnosed. These conditions may be more obvious in very young children, as the obesity is often extreme and can onset in early infancy. Although there are very few patients currently identified in the United States with these deficiencies (~20), Rhythm Pharmaceuticals estimates there may be around 100 to 500 U.S. patients with POMC- or PCSK1- deficiency obesity and around 500 to 2000 U.S. patients with LEPR-deficiency obesity.
Patients with these deficiencies suffer from extreme hunger (hyperphagia) and early-onset severe obesity. Additionally, patients with POMC and PCSK1 deficiency can also suffer from adrenal insufficiency, hypothyroidism, and hypogonadism. These patients often have red hair and pale skin, a helpful indication for a provider to test for a genetic variant. Variants in *LEPR* are associated with hypogonadotropic hypogonadism, hypothyroidism, growth hormone deficiency, and a high risk of infections.
Imcivree represents the first and only FDA-approved treatment for patients with obesity due to POMC, PCSK1, and LEPR deficiency. Imcivree is an MC4R agonist that is intended to partially or completely restore signaling at the MC4R, which is impacted by these deficiencies. Other obesity drugs on the market do not target the underlying cause of obesity in the case of these patients. As a result, other obesity management therapies (Saxenda, Contrave, Qsymia, etc.) are not considered therapeutic alternatives to Imcivree.

Bardet-Biedl syndrome (BBS) is a genetic condition that impacts multiple body systems. It is classically defined by six features. Patients with BBS can experience problems with obesity, specifically with fat deposition along the abdomen. They often also suffer from intellectual impairments. Commonly, the kidneys, eyes and function of the genitalia will be compromised. People with BBS may also be born with an extra digit on the hands.

CONTRAINDICATIONS/EXCLUSIONS/DISCONTINUATION:
Contraindications to Imcivree (setmelanotide) include: Prior serious hypersensitivity to setmelanotide or any of the excipients in Imcivree.

OTHER SPECIAL CONSIDERATIONS:
None

CODING/BILLING INFORMATION

Note: 1) This list of codes may not be all-inclusive. 2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

HCPCS CODE	DESCRIPTION
NA	

AVAILABLE DOSAGE FORMS:
Imcivree SOLN 10MG/ML multiple-dose vial

REFERENCES

1. Imcivree (setmelanotide) [prescribing information]. Boston, MA: Rhythm Pharmaceuticals; November 2023.
2. National Institutes of Health. In NIH trial, Setmelanotide for the Treatment of Early-Onset POMC Deficiency Obesity (Study 1, NCT02896192). www.clinicaltrials.gov. Published September 2016. Updated January 2021.
3. National Institutes of Health. In NIH trial, Setmelanotide for the Treatment of LEPR Deficiency Obesity (Study 2, NCT03287960). www.clinicaltrials.gov. Published September 2017. Updated January 2021.
4. Richards S, Aziz N, Bale S, et al; ACMG Laboratory Quality Assurance Committee. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. *Genet Med*. 2015;17(5):405-424. doi:10.1038/gim.2015.30
5. Clément K, van den Akker E, Argente J, et al. Efficacy and safety of setmelanotide, an MC4R agonist, n individuals with severe obesity due to LEPR or POMC deficiency: single-arm, open- label, multicentre, phase 3 trials. *Lancet Diabetes Endocrinol.* 2020;8(12):960-970. doi:10.1016/S2213-8587(20)30364-8
6. Rhythm Pharmaceuticals Announces FDA Approval of IMCIVREE™ (setmelanotide) as First- ever Therapy for Chronic Weight Management in Patients with Obesity Due to POMC, PCSK1 or LEPR Deficiency. News release. Rhythm Pharmaceuticals, Inc. November 27, 2020. Accessed February 4, 2021. https://ir.rhythmtx.com/news-releases/news-release- details/rhythm-pharmaceuticals-announces-fda-approval-imcivreetm
7. Parisi, X. (2022, July 12). Bardet-Biedl syndrome. Retrieved December 30, 2022, from https://rarediseases.org/rare-diseases/bardet-biedl-syndrome/

SUMMARY OF REVIEW/REVISIONS	DATE
REVISION- Notable revisions: Contraindications/Exclusions/Discontinuation References	Q3 2024
REVISION- Notable revisions: Drug Class	Q3 2023
REVISION- Notable revisions: Diagnosis FDA-Approved Uses Background Contraindications/Exclusions/Discontinuation Available Dosage Forms References	Q1 2023
Q2 2022 Established tracking in new format	Historical changes on file